Serial No.: 09/747,004
Attorney Docket No.: 3366.1

REMARKS

Claim Rejections under 35 U.S.C. §103 should be Withdrawn

1. Claims 1-16, 18 & 20-24 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Urdea et al. (US Patent No. 4,868,105; 1989) in view of Lockhart et al. (US Patent No. 6,040,138; 2000). Applicants respectfully disagree with the Office Action.

Urdea et al. discuss methods for detecting a single analyte using a labeling probe set and a capturing probe set. An analyte is bound by multiple probes in multiple regions (Figure 1). Urdea et al. do not motivate or suggest detection of a plurality of targets/analytes using at least 50 mediator probes and at least 50 different cipher probes, as recited in Claims 1-16, 18 & 20-24 of the invention.

Lockhart et al. teach expression monitoring on high density arrays in which more than 100 different oligonucleotides may be bound. The Examiner alleges that one of ordinary skill in the art would have been motivated to combine Lockhart et al's multiple probes and lengths to Urdea et al's assay in order to detect a multiplicity of genes. Applicants respectfully disagree and submit that the Office Action failed to point out any suggestion to combine the references. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art (Urdea et al.) also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680. The complex design of Urdea et al's detection method in which the recognition sites for the capture probes lie between the recognition sites for the labeling probes (Column 3, lines 1-8 and Column 4, lines 1-5) would not motivate one of ordinary skill in the art to extrapolate the method to a plurality of targets where the complexity increases manifold.

In addition, in the method recited in Urdea et al., the labeling probes are first bound to the analyte under annealing conditions and the analyte complex solution is subsequently added to the solid support bearing the capturing probes (Column 6, lines 25-33). In contrast, the presently claimed methods recite detection of a plurality of targets wherein hybridization of the targets to the mediator probes occurs on the cipher probe-bearing solid support itself. Urdea et al., in Column 2 lines 24-30, teach away from this in reciting

> "By providing for annealing of nucleic acid sequences in solution, the time for performing the assay can be substantially diminished as compared to annealing on a solid surface....., so as to reduce technician error."

Moreover, as stated in the Response dated July 14th 2003, the primary advantage of the Claimed methods is the flexibility of the assay, i.e., one type of array can be used as a universal array to detect different sets of targets by using different mediator probes. In addition, adding a large number of mediator probes increases the complexity of microarray-based assays and places the Claimed methods much above the level of one of ordinary skill in the art.

Applicants respectfully submit that in view of the above arguments, the rejection of Claims 1-6, 18 and 20-24 under 35 U.S.C. §103(a) should be withdrawn.

2. Claims 17 and 19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Urdea et al. in view of Lockhart et al. and further in view of Vinayak et al. (US Patent No. 4,868,105; 2001). For reasons same as the ones stated above, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of obviousness and request that the rejection of Claims 17 and 19 under 35 U.S.C. §103(a) be withdrawn.

3. Claims 1-16, 18 and 20-24 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Southern et al. (US Patent No. 6,150,095; 2000) in view of Lockhart et al. Applicants respectfully disagree with the Office Action.

Southern et al. discuss a method of detecting genetic variations with an allele-specific oligonucleotide (ASO) probe bound to a support that forms a duplex with a target and using ligase or polymerase to extend one chain of the duplex. The Examiner alleges that one of ordinary skill in the art would have been motivated to apply Lockhart's teachings of 100 different oligonucleotides to Southern's method of analyzing sequences in order to detect multiple samples. As explained above, the Examiner has failed to point out the motivation or suggestion in the prior art to combine the two references. Therefore, the rejection of Claims 1-16, 18 and 20-24 under 35 U.S.C. §103(a) should be withdrawn.

4. Claims 17 and 19 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Southern et al. in view of Lockhart et al. and further in view of Vinayak et al. Applicants respectfully disagree with the Office Action and submit that the Examiner has failed to establish a *prima facie* case of obviousness. Therefore the rejection of Claims 17 and 19 under 35 U.S.C. §103(a) should also be withdrawn.

Claim Rejections under 35 U.S.C. §112 should be Withdrawn

Claims 1-24 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Specifically, the Examiner alleges that Claims 1-14 are indefinite because it is unclear as to whether the mediator nucleic acids would be different. Applicants wish to

clarify and concur with the Examiner that the mediator nucleic acids would be inherently different as they would bind to 50 different cipher probes and 50 different targets.

The Examiner also alleges that Claims 21-24 are indefinite because the claims recite a specific number of cipher and mediator oligonucleotides to each nucleic acid target whereas the parent claim recites 50 different target nucleic acids, thereby allegedly making it unclear as to how the different mediator probes bind to the same target when they are to bind to different targets. Applicants respectfully wish to clarify that the different mediator probes do indeed bind to different targets. However, each target could also have more than 1 mediator and/or cipher probe designed to bind to it so as to increase the accuracy of detection. Thus, for example, 50 targets might have 50 different mediator/ cipher probes directed to them or 150/250/500/1000 different mediator/cipher probes directed to them.

In view of the above remarks, Applicants respectfully submit that the rejection of Claims 1-24 under 35 U.S.C. §112 should be withdrawn.

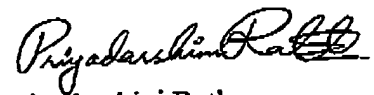
CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned agent.

Respectfully submitted,



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Limited Recognition under 37 CFR 10.9(b)

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